

Identification of putative endothelial progenitor cells (CD34+CD133+Flk-1+) in endarterectomized tissue of patients with chronic thromboembolic pulmonary hypertension.

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Public Summary:

Scientific Abstract:

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by a fibrotic thrombus persisting and obliterating the lumen of pulmonary arteries; its pathogenesis remains poorly defined. This study investigates a potential contribution for progenitor cell types in the development of vascular obliteration and remodeling in CTEPH patients. Endarterectomized tissue from patients undergoing pulmonary thromboendarterectomy was collected and examined for the structure and cellular composition. Our data show an organized fibrin network structure in unresolved thromboemboli and intimal remodeling in vascular wall tissues, characterized by smooth muscle alpha-actin (SM-alphaA)-positive cell proliferation in proximal regions (adjacent to thromboemboli) and neoangiogenesis/recanalization in distal regions (downstream from thromboemboli). Cells that are positively stained with CD34 and fetal liver kinase-1 (Flk-1) (CD34(+)Flk-1(+)) were identified in both the proximal and distal vascular tissues; a subpopulation of CD34(+)Flk-1(+)CD133(+) cells were further identified by immunostaining. Triple-positive cells are indicative of a population of putative endothelial progenitor cells or potential colony-forming units of endothelial cells. In addition, inflammatory cells (CD45(+)) and collagen-secreting cells (procollagen-1(+)) were detected in the proximal vascular wall. Some of the CD34(+) cells in CTEPH cells isolated from proximal regions were also positive for SM-alphaA. Our data indicate that putative progenitor cell types are present in the neointima of occluded vessels of CTEPH patients. It is possible that the microenvironment provided by thromboemboli may promote these putative progenitor cells to differentiate and enhance intimal remodeling.

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